

U.S.S.N. 09/139,425
Filed: August 25, 1998
AMENDMENT AND RESPONSE TO OFFICE ACTION

In the Claims

91 1. (currently amended) A method for selectively delivering a molecule ~~molecules~~ to the nucleus of endothelial cells of the large vessels, comprising
administering a conjugate of ~~an agent binding selectively to endothelial protein C receptor (EPCR) and the molecule to be delivered to large vessel endothelial cells, wherein the molecules are delivered to the nucleus of the large vessel endothelial cells, wherein the~~
conjugate comprises an agent binding selectively to endothelial protein C receptor (EPCR) which causes uptake by the cell and transfer into the nucleus conjugated to the molecule to be delivered

2. (original) The method of claim 1 wherein the conjugate is formed between the molecule to be delivered and an antibody to EPCR.

3. (original) The method of claim 1 wherein the conjugate is formed between the molecule to be delivered and activated protein C.

4. (original) The method of claim 1 wherein the conjugate comprises a chimeric antibody binding to the molecule to be delivered and to EPCR.

5. (original) The method of claim 1 wherein the molecule to be delivered is a nucleic acid molecule and the nucleic acid molecule is a gene or cDNA under the control of a promoter expressed in the nucleus of an endothelial cell and the nucleic acid molecule is delivered by directly contacting the endothelial cells of large vessels with the nucleic acid molecule conjugate or by catheterization to the endothelial cells.

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6. (original) The method of claim 5 wherein the nucleic acid molecule is selected from the group consisting of triplex forming oligonucleotides, ribozymes, guide sequences for ribozymes, and antisense.
7. (currently amended) The method of claim 1 wherein the molecule to be delivered is selected from the group consisting of drugs, ~~other than nucleic acids and proteins and~~ diagnostic agents, wherein the drug is not a nucleic acid.
8. (original) The method of claim 1 wherein the molecule to be delivered is a protein.
9. (original) The method of claim 8 wherein the protein is a transcription factor.
10. (original) The method of claim 1 wherein the molecule to be delivered is coupled to the agent which binds to EPCR by molecules selected from the group consisting of streptavidin and biotin, and molecules having multiple positive charges.
11. (original) The method of claim 1 wherein the conjugate is administered to large vessel endothelial cells in culture or isolated from an individual.
12. (currently amended) The method of claim 1 wherein the conjugate is administered directly to the cells of to an individual ~~in need of treatment or diagnosis.~~
13. (currently amended) A conjugate of an agent binding selectively to endothelial protein C receptor (EPCR) selected from the group consisting of protein C, activated protein C, antibodies reactive with EPCR and fragments of the antibodies reactive with EPCR binding to EPCR, and a molecule selected from the group consisting of nucleic acids, proteins, and drugs

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~~and diagnostic agents~~ to be delivered to a large vessel endothelial cell, wherein the molecule is not a diagnostic label, wherein the conjugate is a chemical conjugate, fusion protein or conjugate formed by indirect binding by a positively charged polymer, chimeric antibody or streptavidin.

14. (currently amended) A conjugate of

G¹ an agent binding selectively to endothelial protein C receptor (EPCR) selected from the group consisting of an antibody to EPCR, or a fragment or recombinant molecule based ~~ef~~ on the antibody to EPCR, and to

a molecule to be delivered to a large vessel endothelial cell, wherein the molecule is not a diagnostic label,

wherein the conjugate is a chemical conjugate, fusion protein or conjugate formed by indirect binding by a positively charged polymer, chimeric antibody or streptavidin.

15. (previously amended) The conjugate of claim 13 wherein the conjugate is formed between the agent to be delivered and activated protein C.

16. (original) The conjugate of claim 13 wherein the molecule to be delivered is a nucleic acid molecule in combination with means for directly contacting the nucleic acid molecule conjugate directly with the endothelial cells of large vessels, wherein the means are for in vitro treatment of the cells or by catheterization to the endothelial cells.

17. (original) The conjugate of claim 16 wherein the nucleic acid molecule is a gene or cDNA under the control of a promoter expressed in the nucleus of an endothelial cell.

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18. (original) The conjugate of claim 16 wherein the nucleic acid molecule is selected from the group consisting of triplex forming oligonucleotides, ribozymes, guide sequences for ribozymes, and antisense.

19. (currently amended) The conjugate of claim 13 wherein the molecule to be delivered is a drug ~~other than nucleic acids and proteins~~, wherein the drug is not a nucleic acid or protein.

20. (original) The conjugate of claim 13 wherein the molecule to be delivered is a protein.

21. (previously amended) The conjugate of claim 20 wherein the protein is a transcription factor.

22. (previously amended) The conjugate of claim 20 comprising a coupling means which binds the molecule to be delivered to the agent which binds EPCR.

23. (original) The conjugate of claim 22 wherein the coupling means is a positively charged polymer or molecule.

24. (original) The conjugate of claim 22 wherein the coupling means is streptavidin-biotin.

25. (previously amended) The conjugate of claim 13 comprising a chimeric antibody which binds to EPCR and to the molecule to be delivered.

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